REMARKS

Applicants have canceled withdrawn claims 1 and 8-22 without prejudice. Applicants have also deleted certain embodiments under R^2 in claims 2-3 to advance prosecution. Applicants reserve the right to pursue cancelled subject matter in subsequent applications claiming benefit herefrom. Applicants have amended claims 2, 5, 6 and 7 to correct formalities and dependencies. No new matter has been added.

Claim Objections

The Examiner has objected claim 1 for containing non-elected subject matter.
Applicants have cancelled claim 1, therefore, the rejection is moot.

The Examiner has objected claims 5 and 6 for a Markush group written in improper format.
Applicants have amended claims 5 and 6 to insert "and" to correct the formality.

Claims Rejections under 35 USC § 112 1st paragraph

Written Description

The Examiner rejects claims 1-4 and 7 under 35 USC § 112 1st paragraph as failing to comply with the written description requirement. The Examiner contends that (i) substantial structural variation exists in the genus/subgenus ; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function is neither disclosed nor commonly known. The Examiner cites *Regents of the University of California v. Eli Lilly & Co.* and *In re Gostelli* for support.

In particular, the Examiner contends that the claimed R^2 and R^5 under Formula II is broader than what is supported by the disclosure. The Examiner contends that the compounds reduced to practice support the following definitions for the variables:

R^2: $N(R^4)_2$ wherein R^4=hydrogen or unsubstituted alkyl

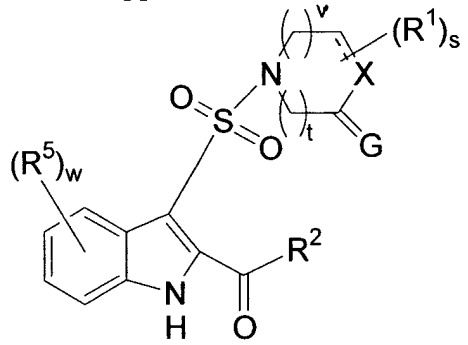
R^5: all variables with the following limitations

- R^a is hydrogen; unsubstituted alkyl
- R^6 is hydrogen; unsubstituted alkyl; alkyl substituted with phenyl/pyridinyl, phenyl or pyridinyl
- For R^5 = options 1-5, 7-10, 12-22
  - R^4 is hydrogen; unsubstituted alkyl; alkyl substituted with R^7= unsubstituted alkyl, halogen, CF_3
- For R^5 = options 6 and 11

- R^4 is hydrogen; unsubstituted alkyl; alkyl substituted with R^7 = unsubstituted alkyl, halo, CF_3, phenyl, pyridinyl, pyrazinyl, furanyl, benzofuranyl, thienyl, benzothienyl, thiazolyl, isoxazolyl, pyrrolyl; phenyl; pyridinyl; pyrazinyl; furanyl; benzofuranyl; thienyl; benzothienyl; thiazole; isoxazolyl; pyrrolyl

Applicants traverse. A claim to a genus may be sufficiently described without describing all species that the claim encompasses. See *Utter v. Hiraga*, 845 F. 2d 993, 998-99 (Fed. Cir. 1988). In *University of California*, the court ruled that a description of a genus may be achieved by means of a recitation of representative number of species or a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See *University of California*, 119 F. 3d at 1569.

Applicants claim compounds under Formula II.



II

Formula II describes a core structural feature common to all members of the genus. The core structural feature contributes to a substantial portion of the genus of molecules in three-dimensional space or molecular weight. The genus allows for limited variations in R^2 and R^5.

In addition, the facts here are distinguishable from *In re Gostelli*. *In re Gostelli* pertains to a priority application describing two species without describing a genus. Here, a genus with a core structure is described, and more than 200 compounds under the genus are described.

Therefore, claims 1-4 and 7 satisfy the written description requirement.

However, in order to advance prosecution, applicants have amended R^2 to NH_2 without prejudice. Applicants have modified the Examiner's summary of compounds reduced to practice that support R^5.

R^6 is hydrogen; unsubstituted alkyl; alkyl substituted with R^7, R^7 is substituted or unsubstituted aryl or substituted or unsubstituted heterocycle. Support for the underlined embodiment is found for example, in examples 63, 86, 89 and 90. Applicants have described a representative number of species (4 examples) under this embodiment.

For R^5 = options 1-5, 7-10, 12-22,

R^4 is hydrogen; unsubstituted alkyl; alkyl substituted with R^7=unsubstituted alkyl and halogen.

For R^5 = options 6 and 11,

R^4 is hydrogen; unsubstituted alkyl; aryl or heterocycle optionally substituted with R^7, R^7 is unsubstituted alkyl. Support for the underlined embodiment is found for example, in example 43 for phenyl, examples 44 and 65 for phenyl, examples 67, 68 and 73 for pyridinyl, example 66 for pyrazinyl, examples 42 and 70 for furanyl, example 69 for benzofuranyl, example 57 for thienyl, example 76 for benzothienyl, example 74 for thiazolyl, example 71 for substituted isoxazolyl, example 72 for pyrrolyl. Applicants have described a representative number of species (15 examples) under this embodiment.

Enablement

The Examiner contends that claims 1-4 and 7 lack enablement. The Examiner contends that that the specification is not enabling for the use of the compounds, and pharmaceutical compositions thereof, that are not supported by the disclosure. The Examiner cites Velaparthi et al. to show that the level of predictability in the art is low since modest structural changes effect noticeable changes to the activity, and concludes that it is not known what structural modifications within the unrepresented genus, would lead to compounds that are active.

Applicants traverse. First of all, Velaparthi describes a class of benzoimidazol-pyridinone tyrosine kinase inhibitors with a completely different core structure, which would have a different mode of binding to the insulin-like growth factor, and thus a different structure-activity profile.

Second, on pages 187-188 of the specification, applicants teach how to test compounds for IGF-1R receptor kinase activity via enzyme reaction and a cell-based autophosphorylation assay. Therefore, one can readily test the activity of the exemplified compounds, and correlate structure and activity through tabulating compounds by different class and types of substituents and comparing activity level. This testing and deduction of the correlation involves some experimentation but it is not undue.

Applicants submit herewith Exhibit 1: Matsuno et al., J. Med. Chem. 2002, 45, 3057-3066; which shows by the priority date of the application, it was ordinary skill in the art to deduce the structure-activity relationship by testing the activity of the compounds and making comparisons of structure and activity. *See* Tables 1-3, and "SAR for Inhibition of beta-PDGFR Phosphorylation" Section of Matsuno et al. Therefore, one of ordinary skill could readily determine which structural limitations are required for preservation of activity.

Therefore, applicants request withdrawal of the rejection under 35 USC § 112 1st paragraph.

Claims Rejections under 35 USC § 112 1st paragraph

The Examiner contends that claim 2 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner contends that the definition of Formula II encompasses compounds wherein the carbon atom of the Markush alternative X has an incomplete valence.

As in conventional chemical compound drawings, hydrogen is usually not included for C atoms in the drawing for simplification. However, a person of ordinary skill in the chemical arts would understand that C has hydrogens attached to reach a complete valence of 4. Applicants have also chosen not to use CH_2 and NH to define X because of the optional double bond attached to the X atom.

When R^1 s=0 and X=C, one skilled in the art would understand that C is attached to two hydrogens; and if there is an optional double bond, then C is attached to one hydrogen.

When X=C and R^1 $_{s\geq 1}$, wherein R^1 substitutes a carbon other than X, one skilled in the art would understand that a C is either substituted by 1) one R^1 and having a hydrogen attached to complete the valence of 4; 2) two R^1; or not substituted but having two hydrogens attached to complete the valence of 4; and if there is an optional double bond for the C, then the C is either substituted by 1) one R^1; 2) not substituted but having one hydrogen attached to complete the valence of 4.

Applicants have deleted H from R^1 to clarify this point.

Therefore, applicants request withdrawal of the rejection under 35 USC § 112 2nd paragraph.

If a telephonic communication with Applicant's representative will aid in the advancement of the prosecution of this application, please telephone the representative indicated below.

Respectfully submitted,

By: _____

Li Su
Registration No. 45,141
Attorney for Applicants

MERCK & CO., INC.
P.O. Box 2000 - RY 60-30
Rahway, New Jersey 07065-0907
Telephone No. (732) 594-5455

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